UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/562,866 | 05/16/2006 | Bror Morein | 1876.052US1 | 6747 |

21186 7590 12/01/2009

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

| EXAMINER | |
|---|---|
| ARCHIE, NINA | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 12/01/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com
request@slwip.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/562,866 | MOREIN ET AL. | |
| | Examiner | Art Unit | |
| | Nina A. Archie | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***DETAILED ACTION***

1. This Office is responsive to Applicant's amendment and response filed 8-11-09. Claims 1-5 and 7-14 are pending and under examination. Claims 1, 4-5, 7, and 9-13 have been amended. Claim 6 is cancelled.

The declaration under 37 CFR 1.132 filed 8/11/2009 by Karin Lovegren Bengtsson dated 8/6/2009 is considered.

***Objections/Rejections Withdrawn***

2. In view of the Applicant's amendments and remarks the following objections/rejections are withdrawn.

a) Objection to claims 1-5 and 7-14 because said claims contained the acronym "iscom" only, is withdrawn in light of applicant's amendment thereto and in light of cancellation of the claim 6.

b) Rejection of claims 1, 4-7, and 11-13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in light of applicant's amendment thereto and in light of cancellation of the claim 6.

c) Rejection of claims 11-13 under 35 U.S.C. 112, first paragraph (written description), is withdrawn in light of applicant's amendment thereto and in light of cancellation of the claim 6.

***Claim Rejections Maintained***

***35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The rejection of claims 1-2, 4-9, and 14 under 35 U.S.C. 102(b) as being anticipated by Friede et al (US Patent No. 6,558,670 Publication Date May 6, 2003) is maintained for the reasons set forth in the previous office action.

**Applicant arguments**:

Applicants arguments filed in response to the 35 U.S.C. 102(b), August 11, 2009 is carefully considered, but not found to be persuasive for the reasons below.

A) Applicants argue there is a difference in the saponin Fraction A of Quil A, which must be present in Applicant's invention, and the closest Fraction QS 7 mentioned in Freide et al. Applicants state Fraction A is composed of several Quil A saponins among them QS 4, 5, 6 and 7, see US Pat No. 5,057,540 (Kensil et al.; enclosed herewith for the Examiner's convenience). Applicants argue Fraction A of Quil A used according to the present invention is not hemolytic and the saponin that Friede et al. prefer and use and in column 2, lines 19-22, refer to the hemolytic saponins QS21 and QS17 of US Pat. No. 5,057,540. Figure 10 of US Pat. No. 5,057,540 shows that QS21 and 17 are indeed hemolytic at around 10/zg/ml. Applicants state Morein, and other experts have described in numerous articles that the hemolytic activity of the saponins is abolished by the incorporation into ISCOM structures evidenced by Drane et al., Expert Rev Vaccines 6(5), 772, 2007 (page 762 left column lines 22-25; a copy of which is enclosed herewith for the Examiner's convenience).

B) Applicant argue Fraction A shown in declaration (enclosed herewith) executed by Inventor Karen Lovegren Bengtsson is obtained by a different method than the Fraction QS7 and is more crude in that it among other Fraction s also comprises Fraction QS 7. Applicants argue saponin Fraction A of Quil A of the present invention has a different effect than Fraction QS 7 mentioned in Friede et al. Applicants argue there is a difference in the saponin Fraction A of Quil A that must be present in Applicant's invention and Fraction C of Quil A comprising Fraction QS 21 containing other saponins other than QS 21 tested in the example of the Friede et al. Applicants argue the difference between Fraction A of Quil A and Fraction QS 21 tested in Friede et al. is the type of immunological reaction induced. Applicant provided in the Declaration titled "Intranasal administration of PR8 micelles," as an attachment results from an assay in which Applicant tested Fraction A and C from Quil A in an intranasal administration of Fraction A in free form. It is evident from the results that Fraction A of Quil A does not improve the IgA titre (columns 2, 3 and 4 of the figure) after intranasal administration which confirms the intranasal adjuvant effect of Fraction C comprising Fraction QS 21 and other saponins which had no effect shown with Fraction A.

**Examiner Response to Applicants Arguments**:

In response to applicant's statement in (A) as set forth supra, the claims are drawn to a method of enhancement of an immune response and immunomodulating activity comprising intraperitoneally or subcutaneously administering to a subject an effective amount of an adjuvant composition with synergistic effect comprising an immunostimulating complex (ISCOM) particles comprising Fraction A of Quil A together with at least one other adjuvant, wherein the at least one other adjuvant is in free form or integrated into another separate ISCOM particles other than the ISCOM particles in which one Fraction A of Quil A is integrated. In response to Applicants argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., hemolytic) are not recited in the rejected claim(s) and the claims are not specifically limited to any hemolytic saponin. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The specification does not state what constitutes Fraction A of Quil A in comparison to the prior art. Therefore, Examiner interprets the claim to comprise Fraction A of Quil A with at least one other adjuvant in free form or to comprise Fraction A of Quil A with at least one other adjuvant integrated into another separate ISCOM other than the ISCOM in which Fraction A of Quil A is integrated as directed to the instant claims.

In response to applicant's statement in (B) as set forth supra, the Declaration signed by Inventor Karen Lovegren Bengtsson is not commensurate in scope because the claims are not specifically limited a method of intranasal administration Fraction A and C from Quil A thus the Declaration is deemed unpersuasive. Eventhough Applicant discloses in the Declaration Fraction A and Fraction C of Quil A, said Fractions of A and C do not disclose the materials that make up each fraction and are not materially different than the prior art of Friede et al. Therefore Fraction A of Quil A of in the instant invention is deemed to be the same as a result of no material distinction with Friede et al and the disclosure in the Declaration. Furthermore, in response to applicant's argument of a difference in immunological responses between Fraction A of Quil A and Fraction QS 21 and Fraction A and Fraction QS7 obtained by different methods, the fact that applicant has recognized another advantage which would flow naturally from following the

suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

As outlined previously, the instant claims are drawn to a method of enhancement of an immune response and immunomodulating activity comprising intraperitoneally or subcutaneously administering to a subject an effective amount of an adjuvant composition with synergistic effect comprising an immunostimulating complex (ISCOM) particles comprising Fraction A of Quil A together with at least one other adjuvant, wherein the at least one other adjuvant is in free form or integrated into another separate ISCOM particles other than the ISCOM particles in which one Fraction A of Quil A is integrated (claim 1) wherein at least one other adjuvant is monophosphoryl lipid A (claim 2), wherein said at least one other adjuvant is integrated into one ISCOM particles (claim 4), wherein said Fraction A of Quil A is integrated into ISCOM particles and said at least one other adjuvant is integrated into ISCOM particles other than the ISCOM particles in which Fraction A of Quil A is integrated (claim 5), wherein said Fraction A of Quil A is integrated into one ISCOM particle and said at least one other adjuvant is not integrated into ISCOM particle (claim 7), wherein said at least one other adjuvant is at least one of monophosphoryl lipid A and cholera toxin CT (claim 8), wherein said ISCOM particle is an ISCOM complex (claim 9), wherein the composition further comprises a pharmaceutically acceptable carrier, diluents, excipient or additive (claim 14).

Friede et al teach a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect (see column 3 lines 1-5, see column 10 lines 30-60), comprising: an ISCOM particle comprising Fraction A of Quil A; and together with at least one other adjuvant (CpG) (see example 1). Friede et al teach that the CpG used in the adjuvant combinations (see column 3 lines 25-65) of the present invention may be in free solution or may be complexed to ISCOMs (see column 9 lines 30-67). Friede et al teach that the CpG and saponin in the adjuvants or vaccines of the present invention may be separate or associated (see column 9 lines 30-67). Friede et al teach that the hemolytic saponin preparations will further be combined with other adjuvants including Monophosphoryl Lipid A (see columns 9 lines 50-56) therefore the method of Fried et al teach the method according to claim 1 wherein said one other adjuvant is monophosphoryl lipid A and the method according to claim 7 wherein said at least

one other adjuvant is at least one of Monophosphoryl Lipid A. Friede et al teach the method wherein said ISCOM particle is an ISCOM complex (Quil A, cholesterol, adjuvant), (see column 8 lines 60-65, column 4 lines 9-15) wherein in the composition further comprises a pharmaceutically acceptable carrier (see abstract, see column 10 lines 65-67). Friede et al teach the newly added limitations "intraperitoneally or subcutaneously administering" (see column 8 lines 46-54).

Therefore, Friede et al anticipates all the claim limitations of the rejected claims.

***35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The rejection of claims 1-14 under 35 U.S.C. 103(a) as being unpatentable over Friede et al (U.S. Patent No. 6,558,670) in view of Cox et al (WO 96/11711) is maintained for the reasons set forth in the previous office action.

**Applicant arguments**:

Applicants arguments filed in response to the 35 U.S.C. 103(a), August 11, 2009 is carefully considered, but not found to be persuasive for the reasons below.

Applicants argue Fraction A of Quil A is not mentioned at all in Friede et al. Applicants argue Fraction A of Quil A is not hemolytic which is evident from the cited Cox patent application WO 96/11711 (see Table 1 on page 8 of WO 96/11711 disclosing that Fraction A has

very low hemolytic activity). Applicants argue Friede et al. teaches away from using Fraction A of Quil A, as Fraction A is not hemolytic. Applicants state Friede et al mentions that the saponin may be in the form of ISCOM col. 5 lines 8-10. Applicants argue Cox et al relates only to the integration of fractions in the same ISCOM complex. Applicants argue experts have described in numerous articles that the hemolytic activity of the saponins is abolished by the incorporation into ISCOM structures. Applicants argue Friede et al. teach away from using ISCOMs, as Friede et al. clearly state that hemolytic saponins are preferred.

**Examiner Response to Applicants Arguments**:

In response to applicant's statement as set forth supra, in regards to Applicants arguments that the references fail to show certain features of Applicant's invention, it is noted that the features upon which applicant relies (i.e., hemolytic) are not recited in the rejected claim(s) and the claims are not specifically limited to any hemolytic saponin. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the specification does not state what constitutes Fraction A of Quil A in comparison to the prior art. Therefore, Examiner interprets the claim to comprise Fraction A of Quil A with at least one other adjuvant in free form or to comprise Fraction A of Quil A with at least one other adjuvant integrated into another separate ISCOM particles other than the ISCOM particles in which Fraction A of Quil A is integrated. Applicant has not disclosed a material distinction between the Fraction A of Quil A and Friede et al, therefore said Fraction A of Quil A of in the instant invention is deemed to be the same as Friede et al. The method of Cox et al teach a method as claimed comprising an ISCOM particle comprising a Fraction A of Quil A; and together with at least one other adjuvant, in free form or integrated into another separate ISCOM particle, wherein at least one other adjuvant is integrated into one ISCOM particle (see pg. 3 lines 20-30,

pgs. 4-5). Therefore, one skilled in the art would be motivated to use the ISCOM matrix complex (as disclosed by Cox et al) as the ISCOM particle as taught by Friede et al in order to take advantage of the reduced Quil A toxicity associated with the use of said complexes. Furthermore the motivation to combine references can be different than Applicants. Therefore one would be motivated to combine teachings of Friede et al. with Cox et al. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding a obviousness. See the recent Board Decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007 (citing KSR, 82 USPQ2d at 1396) available at (http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

As outlined previously, the instant claims are drawn to a method of enhancement of an immune response and immunomodulating activity comprising intraperitoneally or subcutaneously administering to a subject an effective amount of an adjuvant composition with synergistic effect comprising an immunostimulating complex (ISCOM) particles comprising Fraction A of Quil A together with at least one other adjuvant, wherein the at least one other adjuvant is in free form or integrated into another separate ISCOM particles other than the ISCOM particles in which one Fraction A of Quil A is integrated (claim 1) wherein at least one other adjuvant is monophosphoryl lipid A (claim 2), wherein the saponin fraction from Quil A is Fraction C of Quil A or Fraction B of Quil A (claim 3), wherein said at least one other adjuvant is integrated into one ISCOM particles (claim 4), wherein said Fraction A of Quil A is integrated into ISCOM particles and said at least one other adjuvant is integrated into ISCOM particles other than the ISCOM particles in which Fraction A of Quil A is integrated (claim 5), wherein said Fraction A of Quil A is integrated into one ISCOM particle and said at least one other adjuvant is not integrated into ISCOM particle (claim 7), wherein said at least one other adjuvant is at least one of monophosphoryl lipid A and cholera toxin CT (claim 8), wherein said ISCOM particle is an ISCOM complex (claim 9), wherein said ISCOM particle is an ISCOM matrix complex (claim 10), wherein the composition comprises 50-99.9% of Fraction A of Quil A; and 0.1-50% of the saponin Fraction of Quil A based on the total weight of the composition (claim 11), wherein the composition comprises 75-99.9% of Fraction A of Quil A; and 0.1-25% of the saponin Fraction of Quil A based on the total weight of the composition (claim 12), wherein the composition comprises 91-99.1% of Fraction A of Quil A; and 0.1-9%

of the saponin Fraction of Quil A based on the total weight of the composition (claim 13), wherein the composition further comprises a pharmaceutically acceptable carrier, diluent, excipient or additive (claim 14).

Friede et al teach a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect (see column 3 lines 1-5, see column 10 lines 30-60), comprising: an ISCOM particle comprising Fraction A of Quil A; and together with at least one other adjuvant (CpG) (see example 1). Friede et al teach that the CpG used in the adjuvant combinations (see column 3 lines 25-65) of the present invention may be in free solution or may be complexed to ISCOMs (see column 9 lines 30-67). Friede et al teach that the CpG and saponin in the adjuvants or vaccines of the present invention may be separate or associated (see column 9 lines 30-67). Friede et al teach that the hemolytic saponin preparations will further be combined with other adjuvants including Monophosphoryl Lipid A (see columns 9 lines 50-56) therefore the method of Fried et al teach the method according to claim 1 wherein said one other adjuvant is monophosphoryl lipid A and the method according to claim 7 wherein said at least one other adjuvant is at least one of Monophosphoryl Lipid A. Friede et al teach the method wherein said ISCOM particle is an ISCOM complex (Quil A, cholesterol, adjuvant), (see column 8 lines 60-65, column 4 lines 9-15) wherein in the composition further comprises a pharmaceutically acceptable carrier (see abstract, see column 10 lines 65-67). Friede et al teach the newly added limitations "intraperitoneally or subcutaneously administering" (see column 8 lines 46-54).

Friede et al does not teach a method, wherein the saponin Fraction from Quil A is Fraction C of Quil A or Fraction B of Quil A, wherein ISCOM particle is ISCOM matrix complex, wherein the composition comprises 50-99.9% of Fraction A of Quil A; and 0.1-50% of a fraction or derivative of Quil A based on the total weight of the composition, wherein the composition comprises 75-99.9% of Fraction A of Quil A; and 0.1-25% of a fraction or derivative of Quil A based on the total weight of the composition, wherein the composition comprises 91-99.1% of Fraction A of Quil A; and 0.1-9% of a fraction or derivative of Quil A based on the total weight of the composition.

Cox et al teaches a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect (see pgs. 9-24). The method of Cox et al teaches that an ISCOM matrix can have at least one immunogen (adjuvant), incorporated into or associated with the ISCOM matrix. Therefore the method of Cox et al teach a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an ISCOM particle comprising a Fraction A of Quil A; and together with at least one other adjuvant, in free form or integrated into another separate ISCOM particle, wherein at least one other adjuvant is integrated into one ISCOM particle (see pg. 3 lines 20-30, pgs. 4-5). Cox et al teach the method wherein the saponin Fraction from Quil A is Fraction B of Quil A, wherein said ISCOM particle is an ISCOM complex, wherein said ISCOM particle is an ISCOM matrix complex (see page 7 line 24).

It would have been obvious to one of skill in the art to use the ISCOM matrix complex (as disclosed by Cox et al) as the ISCOM particle as taught by Friede et al in order to take advantage of the reduced Quil A toxicity associated with the use of said complexes.

One would have had a reasonable expectation of success because the ISCOM matrix (as disclosed by Cox et al) has been shown to have a significant adjuvant effect and reduced toxicity as well as (see page 1).

As to dependent claims 11-13 reciting the limitations, "wherein the composition comprises 50-99.9% of Fraction A of Quil A; and 0.1-50% of a fraction or derivative of Quil A based on the total weight of the composition" (claim 11), "wherein the composition comprises 75-99.9% of Fraction A of Quil A; and 0.1-25% of a fraction or derivative of Quil A based on the total weight of the composition"(claim 12), "wherein the composition comprises 91-99.1% of Fraction A of Quil A; and 0.1-9% of a fraction or derivative of Quil A based on the total weight of the composition"(claim 13). Cox et al. teaches saponin preparation of saponins of Quillaja saponaria from 50 to 90% by weight of Fraction A and from 50 to 10% by weight of Fraction C, 50 to 70% by weight of Fraction A and from 50 to 30% by weight of Fraction C, about 70% by weight of Fraction A, about 30% by weight of Fraction C, fractions A, B, and C (page 7, line 24). However, it does not teach the specific percentage weight claimed.

The references also do not specifically teach adding the ingredients in the amounts claimed by applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955). Thus, optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

***New Grounds of Objection***

5. Claims 1-14 is objected to because of the following informalities: As to claim 1 reciting the limitation "another separate ISCOM particles" is contradictory. The term "another" is a singular term whereas particles is a plural term. Appropriate correction is required.

***Conclusion***

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/

for Nina Archie, Examiner of Art Unit 1645